

AUG 17 2004
OFFICIAL

Cooley Godward LLP

ATTORNEYS AT LAW

FAX

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Five Palo Alto Square
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Broomfield, CO
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MAIN (650) 843-5000
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DATE: August 17, 2004

| PLEASE DELIVER TO: | PHONE NO.: | FAX NO.: |
|---|------------|--------------|
| Commissioner for Patents Art Unit 1614 | | 703-872-9306 |

FROM: Tom M. Moran
Reg. No. 26,314

PHONE: (650) 843-5104

REPLY FAX: (650) 857-0663

| | |
|---|----------------------------|
| NUMBER OF PAGES, INCLUDING COVER PAGE: 24 | Client Number: 203177-2474 |
| Originals Will Not Follow | Requestor #: |

MESSAGE:

Re: USSN ~~68~~/082,801

Enclosed are:

- Transmittal (1 p)
- Communication re Notice of Abandonment (1 p)
- Request to Withdraw Notice of Abandonment (2 pp)
- Non-final Office Action dated September 11, 2003 (12 pp)
- Response to the Office Action mailed on March 11, 2004 (7 pp)

If you do not receive all of the pages, please call
Sender's Name at Sender's Phone Number as soon as possible.

Attorney Docket No.: TLIK-048/01US

PATENT

I hereby certify that this correspondence is being transmitted by facsimile addressed to Examiner Kwon, Art Unit 1614, Facsimile Number 703-872-9306, at United States Patent and Trademark Office, Alexandria, VA 22313-1450 on August 17, 2004.

By: Hanna Hacham
Hanna Hacham

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Hugo O. Villar et al. Confirmation No.: 2049
App. No.: 10/082,801 Art Unit: 1614
Filed: 22 February 2002 Examiner: Brian Young S. Kwon

For: ACRIDINES AS STIMULATORS FOR Fas-MEDIATED APOPTOSIS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

WITHDRAW NOTICE OF ABANDONMENT TRANSMITTAL

Enclosed are the following documents in response to the Notice of Abandonment mailed June 29, 2004:

- ☒ Communication re Notice of Abandonment;
- ☒ Request to Withdraw Notice of Abandonment;
- ☒ Non-final Office Action dated September 11, 2003;
- ☒ Response to the Office Action mailed on March 11, 2004.

The Commissioner is hereby authorized to charge any appropriate fees that may be required by this paper to Deposit Account No. 03-3117.

Dated: August 17, 2004

Respectfully submitted,

Cooley Godward LLP
ATTN: Patent Group
Five Palo Alto Square
3000 El Camino Real
Palo Alto, CA 94306-2155
Tel: (650) 843-5000
Fax: (650) 857-0663
TMM/hh

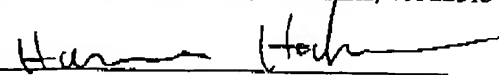
COOLEY GODWARD LLP

By: Tom M. Moran
Tom M. Moran
Reg. No. 26,314

Attorney Docket No.: TLIK-048/01US

PATENT

I hereby certify that this correspondence is being transmitted by facsimile addressed to Examiner Kwon, Art Unit 1614, Facsimile Number 703-872-9306, at United States Patent and Trademark Office, Alexandria, VA 22313-1450 on August 17, 2004.

By: 
Hanna Hacham

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Hugo O. Villar et al. Confirmation No.: 2049
App. No.: 10/082,801 Art Unit: 1614
Filed: 22 February 2002 Examiner: Brian Young S. Kwon

For: ACRIDINES AS STIMULATORS FOR Fas-MEDIATED APOPTOSIS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

COMMUNICATION RE NOTICE OF ABANDONMENT

Upon receiving the facsimile transmission sent August 13, 2004, a clerical error was identified below the signature line on the transmittal document and the "Request to Withdraw Notice of Abandonment."

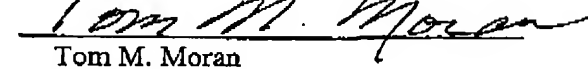
The error is an incorrect Reg. No. The correct Reg. No. for Tom M. Moran is 26, 314. Newly executed documents, which have the correct Reg. No., accompany this communication.

Dated: August 17, 2004

Cooley Godward LLP
ATTN: Patent Group
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3000 El Camino Real
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Tel: (650) 843-5000
Fax: (650) 857-0663
TMM/hh

Respectfully submitted,

COOLEY GODWARD LLP

By: 
Tom M. Moran
Reg. No. 26,314

Attorney Docket No.: TLIK-048/01US

PATENT

I hereby certify that this correspondence is being transmitted by facsimile addressed to Examiner Kwon, Art Unit 1614, Facsimile Number 703-872-9306, at United States Patent and Trademark Office, Alexandria, VA 22313-1450 on August 17, 2004.

By: 

Hanna Hacham

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Hugo O. Villar et al.

Confirmation No.: 2049

App. No.: 10/082,801

Art Unit: 1614

Filed: 22 February 2002

Examiner: Brian Young S. Kwon

For: **ACRIDINES AS STIMULATORS FOR Fas-MEDIATED APOPTOSIS**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REQUEST TO WITHDRAW NOTICE OF ABANDONMENT

In response to the Notice of Abandonment mailed June 29, 2004, this communication is being sent to request the Office to withdraw the Notice of Abandonment as a mistake. The facts in this case are as follows:

- (1) On September 11, 2003, a non-final office action was mailed to Heller Ehrman White & McAuliffe LLP ("Heller" - see document attached - Tab 1).
- (2) On March 11, 2004, Sam Nguyen of Heller successfully faxed a response to the above office action (attached - Tab 2).
- (3) The USPTO was authorized to charge deposit account 08-1641 in the amount of \$950 for an extension of time and other charges, as required. (See Transmittal - Tab 2.)

- (4) The fax transmission was successful as evidenced by the "TX REPORT" on the last page of Tab 2. The start time indicates that the document was sent on 11th of March at 14:14 (2:14 pm). One minute forty-six seconds was used and the number of pages sent was six. Note that the result indicated is "OK". The phone number is consistent with the number used to make the fax transmission.
- (5) The form of the claim amendments is consistent with 37 C.F.R. 1.121, as amended July 30, 2003, with the new material that is added to the claim indicated by underlining and the old material which is deleted being struck through.

Thus, it appears that the evidence is clear the transmittal and the Response to Office Action were sent in a timely manner. The format of the amendments was correct and the Notice of Abandonment should be withdrawn, the Examiner's conclusion in the Notice of Abandonment was wrong, and the Examiner should review the application on its merits.

If the Examiner believes it would be useful to have a telephone conversation with the undersigned attorney, he is requested to call at (650) 843-5104.


Dated: August 17, 2004

Cooley Godward LLP
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Respectfully submitted,

COOLEY GODWARD LLP

By:


Tom M. Moran
Reg. No. 26,314

SKN



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
 United States Patent and Trademark Office
 Address: COMMISSIONER FOR PATENTS
 P.O. Box 1450
 Alexandria, Virginia 22313-1450
 www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/082,801 | 02/22/2002 | Hugo O. Villar | 25352-0022 | 2049 |

25213 7590 09/11/2003

HELLER EHRMAN WHITE & MCAULIFFE LLP
 275 MIDDLEFIELD ROAD
 MENLO PARK, CA 94025-3506

RECEIVED
 SEP 15 2003
 HEWM LLP - P.A.

EXAMINER

KWON, BRIAN YONG S

ART UNIT PAPER NUMBER

1614

8

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

HEWM LLP - SV Office

| | |
|----------------|-----------------|
| Description | RESPONSE TO OIA |
| Due/Rmr | 12/11/03 |
| Final/Deadline | 3/11/04 |
| Initials | DZ |

| | | | | |
|---|--|-------------------------------|-------------------------------|--|
| RECEIVED Office Action Summary SEP 15 2003 COOLEY GODWARD LLP | | Application No. 10/082,801 | Applicant(s) VILLAR ET AL. | |
| Examiner Brian S Kwon | | Art Unit 1614 | | |

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 17 June 2003.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 463 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) 10 and 11 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-9 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5</u> . | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____ |
|--|--|

Application/Control Number: 10/082,801
Art Unit: 1614

Page 2

DETAILED ACTION

Election/Restrictions

1. Applicants election without traverse the Group I, claims 1-9, is acknowledged. Claims 10-11 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

Claims 1-9 are currently pending for prosecution on the merits.

Information Disclosure Statement

2. Enclosed is an initialed copy of PTO 1449 which has been considered for your records, Application No. 10/082,301.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the specific autoimmune disease or hyperplastic disease such as lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinomas, breast carcinomas, prostate cancers, neuroblastomas and gliomas, but does not reasonably provide enablement for autoimmune disease or hyperplastic disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Application/Control Number: 10/082,801
Art Unit: 1614

Page 3

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention relates to a method of treating an autoimmune or hyperplastic disease comprising administering a compound of the formula.

The instant specification defines that "treating" or "treatment" means "preventing the disease from occurring in a mammal which may be predisposed to the disease but does not yet experience or display symptoms of the disease or inhibiting the disease, i.e., arresting its development (page 5, lines 17-20).

(2) The state of the prior art

The compounds of the inventions are acridine derivatives represented by the formula. The prior art recognizes the therapeutic utility of said acridine derivatives as antihypertensives, potassium channel blockers, antiviral agents, monomeric units for dendrimers and potential anticancer and antitumor agents. However, the prior art does not recognizes cure or the

Application/Control Number: 10/082,801
Art Unit: 1614

Page 4

prophylactic utility of the claimed compounds in preventing disease from occurring in a mammal or complete inhibition or elimination of the disease conditions.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high, and no examples exist for efficacy of a single product against vast number of possible conditions or disease generally described as autoimmune or hyperplastic disease. Furthermore, the lack of significant guidance from the specification or prior art with regard to completely inhibiting or preventing autoimmune or hyperplastic disease with the administration of the instant composition makes practicing the claimed invention unpredictable in terms of the prevention of the disease.

(5) The breadth of the claims

The claims are very broad due to the vast number of possible diseases that can be characterized by autoimmune disease or hyperplastic disease.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA

Application/Control Number: 10/082,801
Art Unit: 1614

Page 5

viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of the compounds of the formula to be effective in treating the entire scope of autoimmune disease or hyperplastic disease is insufficient for enablement. The specification provides no guidance, in the way of enablement for an autoimmune or hyperplastic disease other than lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinomas, breast carcinomas, prostate cancers, neuroblastomas and gliomas. Furthermore, the specification provides no guidance, in the way of enablement for preventing said autoimmune or hyperplastic diseases.

(7) The presence or absence of working examples

As stated above, the specification discloses acridine derivatives represented by the formula that are used to treat autoimmune or hyperplastic diseases associated with FAS-mediated apoptosis, namely lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinomas, breast carcinomas, prostate cancers, neuroblastomas and glioma.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation

Application/Control Number: 10/082,801
Art Unit: 1614

Page 6

should proceed.” In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue “painstaking experimentation study” to determine the activity of the compounds in treating or preventing all of disease conditions that are characterized by autoimmune or hyperplastic diseases that would be enabled in this specification.

The instant claims read on all autoimmune or hyperplastic diseases that may or may not be related to FAST-mediated apoptosis, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

For examination purposes, the phrase “treating” is interpreted as “relieving symptoms of the disease”, “reducing the effects of the disease” or “causing regression of the disease”.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 relates to a method of treating an autoimmune or hyperplastic diseases comprising administering the claimed compounds represented by the formula in combination with “an additional form of therapy for said disease state”. It is not clear what is “an additional

Application/Control Number: 10/082,801
Art Unit: 1614

Page 7

form of therapy for said disease state" meant? Does it refer to known conventional form of therapy for autoimmune or hyperplastic disease? Applicant is requested to clarify.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Radzikowski et al. (Archivum Immunologiae et Therapiae Experimentalis, 1969, 17(1), 86-88).

Radzikowski teaches the use of the claimed acridine derivatives represented by the formula (e.g., 9-(dimethylaminopropylamino)-4-methoxyacridine and 9-(dimethylaminopropylamino)-2-methylacridine) for the treatment of hyperplastic disease such as tumor or cancer in mice (i.e., sarcoma and lymphoma), see Table 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Application/Control Number: 10/082,801
Art Unit: 1614

Page 8

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radzikowski et al. (Archivum Immunologiae et Therapiae Experimentalis, 1969, 17(1), 86-88).

The teaching of Radzikowski has been discussed in above 35 USC 102(b) rejection.

The teaching of Radzikowski differs from the claimed invention (i) in the use of 9-[(3-diethylaminopropyl)amino]acridine and (ii) the combination of other known therapy. The claims differ from the prior art by having ethyl substituent in R4 and R5 position. One having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that substitution of ethyl substituent for methyl in R4 and R5 position would not significantly

Application/Control Number: 10/082,801
Art Unit: 1614

Page 9

alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to use of "an additional form of therapy", the examiner determines that the addition of known therapy for the treatment of hyperplastic disease to the compounds of the formula which has been known for the treatment of cancer or tumor are well considered within the skill of the artisan. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petri et al. (Acta Microbiologica Hungarica, 1995, 42 (2), 203-8 in view of Armistead et al. (US 5192773).

Petri teaches the use of the claimed acridine derivatives represented by the formula as an immunomodulating or immunosuppressive agent (abstract; Table 1).

Armistead discloses the use of immunosuppressive compounds for the treatment of autoimmune disorders.

The teaching of Petri differs from the claimed invention in the use of said compounds for the treatment of autoimmune disease. To incorporate such teaching into the teaching of Petri, would have been obvious in view of Armistead who discloses routine knowledge in the art to utilize immunosuppressive agent in treating autoimmune disorders.

One having ordinary skill in the art would have been motivated to administer the claimed acridine derivatives having immunosuppressive property, with the reasonable expectation of

Application/Control Number: 10/082,801
Art Unit: 1614

Page 10

success, to a mammal to treat autoimmune disorders. One having ordinary skill in the art would have been motivated to make such modification to extend the usage of the claimed acridine derivatives in the treatment of autoimmune disorder.

Conclusion

8. No Claim is allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

**ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600**



| INFORMATION DISCLOSURE STATEMENT (37 CFR 1.56, 1.97, and 1.98) | | | | ATTORNEY DOCKET 25352-0022 | | APPLICATION NO. 10/082,801 | |
|--|--------|--|--------------|--|--|-------------------------------|---------------------------------|
| SHEET 1 OF 1 | | | | APPLICANT(S) Hugo O. Villar, et al. | | | |
| | | | | FILING DATE February 8, 2002 | | GROUP 1645 | |
| U.S. PATENT DOCUMENTS | | | | | | | |
| † EX'R INITIAL | REF. # | PATENT NUMBER | DATE (MO/YR) | NAME | | CLASS/ SUBCLASS | FILING DATE (If appropriate) |
| | | | | | | | |
| FOREIGN PATENT DOCUMENTS | | | | | | | |
| † EX'R INITIAL | REF. # | PATENT NUMBER | DATE (MO/YR) | COUNTRY | | TRANSLATION (YES/NO) | |
| Q | 19 | 00/76982 | 12/2000 | PCT | | | |
| OTHER DOCUMENTS | | | | | | | |
| † EX'R INITIAL | REF. # | CITATION (Author, Article Title, Journal/Book Title, Date, Pertinent Pages, etc.) | | | | | |
| Q | 20 | E. Chotkowska et al., "Cytotoxic properties of nitro derivatives of 9-aminoacridine in cultures of <i>Euglena gracilis</i> ", <i>Arch. Immunol. Ther. Exp.</i> , 20(2), 289-294 (1972) | | | | | |
| Q | 21 | C. Radzikowski et al., "A search for antitumor compounds", <i>Arch. Immunol. Ther. Exp.</i> , 17(1), 86-98 (1969) | | | | | |
| Q | 22 | B. Wysocka-Skrezela et al., "Research on tumour inhibiting compounds. Part LXXII. Reduction of 1-nitro-9(3-dimethylaminopropylamino)-acridine by sodium borohydride", <i>Pol. J. Chem.</i> , 55(7-8), 1735-1736 (1981) | | | | | |
| Q | 23 | M. K. Piesterzeniewicz et al., "Inhibition of RNA synthesis <i>in vitro</i> by acridines - relation between structure and activity", <i>Z. Naturforsch.</i> , 53c(5-6), 359-368 (1998) | | | | | |
| Q | 24 | C. Radzikowski et al., "The cytostatic and cytotoxic effect of 1-nitro-9-aminacridine derivatives", <i>Proc. 5th Int'l Congr. Chemother.</i> , 2(1), 263-266 (1967) | | | | | |
| EXAMINER'S SIGNATURE  | | | | DATE CONSIDERED 8-15-9 | | | |
| † EXAMINER: Initial if reference is considered, whether or not citation is in conformance with MPEP 609. Line through citation if not in conformance and not considered. Include copy of this form in next communication to applicant. * If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identified in the statement and relied upon for an earlier filing date under 35 U.S.C. 120. 37 C.F.R. 1.98(d). | | | | | | | |

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PATENTS
Attorney Docket No. 25352-0022

CERTIFICATE OF FACSIMILE TRANSMISSION

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Sam L. Nguyen, Reg. No. 52,496

Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hugo O. Villar et al

: Confirmation No.: 2049

App. No.: 10/082,801

: Art Unit: 1614

Filed: 22 February 2002

: Examiner: Brian Yong S. Kwon

For: Acridines as stimulators for Fas-mediated apoptosis

Commissioner for Patents
PO Box 1450
Alexandria VA 22313-1450

Sir:

TRANSMITTAL

Transmitted herewith is a response to the Office Action mailed 11 September 2003, totaling, together with this Transmittal, 6 pages.

Please charge the fee for a three-month extension of the period for response (\$950), and any other fees that may be necessary, to our deposit account 08-1641, referring to 25352-0022.

Respectfully submitted,

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11 March 2004

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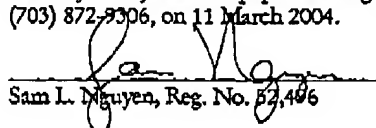
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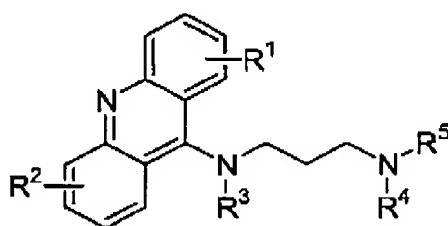
Sir:

RESPONSE TO OFFICE ACTION

In response to the Office Action mailed 11 September 2003, for which a three-month extension of the period for response is requested in the accompanying Transmittal, so that the due date for the response is 11 March 2004, please enter the following amendment and consider the following remarks.

Claim amendments

1. (Currently amended) A method of treating an autoimmune, infectious, or hyperplasic disease selected from autoimmune lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma in a mammal, comprising administering to the mammal a therapeutically effective amount of a compound of the formula:



where:

R¹ and R² are independently selected from hydrogen, halogen, hydroxy, optionally substituted alkyl, optionally substituted alkoxy, ~~NRR'~~ (where R is hydrogen or alkyl and R' is hydrogen, alkyl, or aryl), and optionally substituted aryl; and

R₃, R₄, and R₅ are independently selected from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted alkylcarbonyl, and optionally substituted arylcarbonyl, as a single stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

2. (Canceled)

3. (Currently amended) The method of claim 1, where R³ is hydrogen.

4. (Original) The method of claim 3, where R⁴ and R⁵ are alkyl.

5. (Original) The method of claim 4, where the compound is 9-[(3-diethylaminopropyl)amino]acridine or a pharmaceutically acceptable salt thereof.

6. - 8. (Canceled)

App. No. 10/082,801

Page 3

9. (Currently amended) The method of claim 1, further comprising treating said mammal with an additional form of therapy for said disease ~~state~~, the additional form of therapy being a conventional form of therapy for said disease.

10. - 11. (Canceled)

12. (new) The method of claim 1, where the disease is a hyperplasic disease selected from colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma.

App. No. 10/082,801

Page 4

Remarks

The amendment

Entry of the amendment is respectfully requested.

No new matter is added by the amended/added claims, because each of the claims is supported by the application as filed. Amended claim 1 corresponds to original claim 2 limited to the set of diseases identified at page 1, line 24 – page 2, line 2 as being associated with Fas-mediated apoptosis; amended claim 3 has its dependency changed to reflect the addition of the subject matter of original claim 2 to amended claim 1; and amended claim 9 reflects the additional therapy being conventional for the disease (page 12, line 23). Redundant claims 2 and 6-8 have been canceled; and non-elected claims 10 and 11, withdrawn from consideration, have also been canceled. New claim 12 claims only hyperplastic diseases within the scope of claim 1.

The restriction requirement

Restriction had previously been required between claims 1-9 and 10-11, and Applicants had elected claims 1-9. The non-elected claims have now been canceled.

The 35 USC 112, ¶1 rejection

Original claims 1 and 7 were rejected under 35 USC 112, ¶1 for lack of enablement with respect to the full scope of autoimmune or hyperplastic diseases, while suggesting that the claims were enabled for those diseases reported to be associated with Fas-mediated apoptosis (autoimmune lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma). The Examiner's helpful suggestion has been followed and claim 1, the independent claim, has been amended to limit the diseases to that list. Withdrawal of the rejection is requested.

The 35 USC 112, ¶2 rejection

Original claim 9 was rejected under 35 USC 112, ¶2 for indefiniteness with respect to the "additional form of therapy", while suggesting clarification to a known conventional form of therapy. The Examiner's helpful suggestion has been followed and claim 9 has been amended to specify that the additional therapy be a conventional therapy for the disease (the word "known" has not been included because Applicants believe it is implicit in "conventional"). Withdrawal of the rejection is requested.

The 35 USC 102(b) rejection

Original claims 1-4 and 7 were rejected under 35 USC 102(b) for anticipation by Radzikowski et al., *Archivum Immunologiae et Therapiae Experimentalis*, 1969, 17(1), 86-88 ("Radzikowski"). This rejection, as applied to the amended claims, is respectfully traversed.

The rejection asserts that Radzikowski "teaches the use of the claimed acridine derivatives represented by the formula (e.g. 9-(dimethylaminopropylamino)-4-methoxyacridine and 9-(dimethylaminopropylamino)-2-methylacridine)" for the treatment of hyperplastic disease. Claim 1 has been amended to limit the compounds claimed to only those where the benzene rings of the acridine are unsubstituted, and it is submitted that none of Radzikowski's compounds are unsubstituted. Withdrawal of the rejection is therefore requested.

The 35 USC 103(a) rejections

Original claims 5 and 9 were rejected under 35 USC 103(a) for obviousness over Radzikowski. This rejection, as applied to the amended claims, is respectfully traversed.

App. No. 10/082,801

Page 5

The rejection asserts that the teachings of Radzikowski differ from the claims in the use of 9-[(3-diethylaminopropyl)amino]acridine (claim 5) and combination with other known therapy (claim 9); and that each of these changes would be within the ordinary skill of the art. Applicants disagree. As discussed above with respect to the 35 USC 102(b) rejection, Radzikowski discloses no compounds that are unsubstituted on the benzene rings of the acridine – all are substituted with either methyl or methoxy. Further, as the rejection acknowledges, the closest 9-substitution of Radzikowski is the dimethylaminopropylamino group and not the diethylaminopropylamino group. Applicants submit that Radzikowski fails to suggest that compounds lacking substitution on the benzene rings of the acridine and/or having a diethylaminopropylamino substituent on the 9-position would have efficacy, and the rejection should be withdrawn as to claim 5 for that reason. With respect to claim 9, because Radzikowski discloses no compounds that are unsubstituted on the benzene rings of the acridine and fails to suggest that such compounds would be efficacious alone, there can be no suggestion that they would be efficacious in combination with an other known therapy. Withdrawal of the rejection is therefore requested.

Claim 6 was rejected under 35 USC 103(a) for obviousness over Petri et al., *Acta Microbiologica Hungarica*, 1995, 42(2), 203-208 ("Petri") in view of Armistead et al, US Patent No. 5,192,773 ("Armistead"). Claim 6 has been cancelled.

Conclusion

Entry of the amendment, and examination and allowance of the claims, are respectfully requested.

Respectfully submitted,



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11 March 2004

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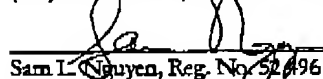
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